Amendments to the Specification

Please replace the paragraph beginning at page 2, line 4, with the following rewritten paragraph:

--We have recently discovered that this hierarchy of polymers can be formed not only by a single type of peptide (homopeptide polymers), but most importantly also by mixing complementary peptides together (alternating co-polymers). For example, we have shown that peptide P11-3 (also known as DN1-2E; SEQ ID NO: 3) (Table 1) adopts monomeric random coil conformation and forms fluid isotropic solutions at pH>7 in water. This behaviour stems from the three glutamate groups on the peptide. At pH higher than their effective pKa, the glutamate side-chains are ionised, and the intermolecular electrostatic repulsions generated by these negatively charged groups prevent beta-sheet self-assembly. Similarly peptide P11-4 (SEQ ID NO: 4) adopts monomeric random coil conformation and forms fluid solutions at pH<7.5 in water. This behaviour stems from the electrostatic repulsions generated between the positively charged ornithine groups (four ornithines per peptide). However, when a solution of P11-3 (SEQ ID NO: 3; negatively charged) is mixed with a solution of P11-4 (SEQ ID NO: 4; positively charged) above a certain critical peptide concentration (typically in the micromolar region), there is instant beta-sheet self-assembly into ribbons, fibrils, or fibres, according to the peptide concentration, and these are formed by an alternating arrangement of the complementary peptides: P11-3 (SEQ ID NO: 3) and P11-4 (SEQ ID NO: 4) etc (Fig.3).--

Please replace the paragraph beginning at page 3, line 11, with the following rewritten paragraph:

-- A material in this aspect of the invention is SAP is P11-1 (SEQ ID NO: 1).--

Please replace the paragraph beginning at page 3, line 21, with the following rewritten paragraph:

--The polar amino acids include from 1 to 3 charged amino acids per 11 amino acids. Preferably, the SAP is selected from the group P11-2 (SEQ ID NO: 2), P11-3 (SEQ ID NO: 3), P11-4 (SEQ ID NO: 4) and P11-5 (SEQ ID NO: 5; also known as DN1-2O).--

Please replace the paragraph beginning at page 4, line 13, with the following rewritten paragraph:

--Preferably, in this aspect of the invention the SAP is P11-3 (SEQ ID NO: 3).--

Please replace the paragraph beginning at page 4, line 26, with the following rewritten paragraph:

--Thus, the SAP may be selected from the group P11-6 (SEQ ID NO: 6) and P10-7 (SEQ ID NO: 7).--

Please replace the paragraphs beginning at page 5, line 10, with the following rewritten paragraphs:

--The tapes, ribbons, fibrils and fibres are increasingly more rigid structures [1]. For example we have found that the persistence length $\tilde{l}$ of single tapes formed by an 11-residue peptide P11-1 (SEQ ID NO: 1) in water is ca 0.3μm, whilst the persistence lengths of ribbons and fibrils formed by a variant P11-2 peptide (SEQ ID NO: 2) in water are 1 and 20-70μm respectively (Table 1).

We have also shown that above a certain peptide concentration $c_{I/N}$ (isotropic to nematic transition concentration) the semi-rigid ribbons, fibrils and fibres can align and thus transform their initially isotropic solution into a nematic liquid crystalline solution . The transition of the solution to the nematic liquid crystalline state happens at lower concentrations for more rigid polymers. For example, the nematic transition for solutions of ribbons of P11-1 (SEQ ID NO: 1) peptide occurs at $c_{I/N} \approx 13$mM, whilst the nematic transition for solutions of the much more rigid fibrils of P11-2 peptide (SEQ ID NO: 2) occurs at $c_{I/N} \approx 0.9$mM.--

Please replace the paragraph beginning at page 5, line 29, with the following rewritten paragraph:

--We have discovered that the alignment of these polymers (tapes, ribbons, fibrils and fibres) can be improved significantly by shearing or application of external magnetic field to the peptide solution. Subsequent gelation locks the aligned polymers into place and preserves their alignment for a long time (typically weeks) even after the polymer solution is removed from the

magnetic field or after the end of shearing. Shearing or external magnetic field (superconducting magnet with a field strength of 7T) have been found indeed to improve the alignment of fibrils in aqueous solutions of P11-2 peptide (SEQ ID NO: 2), as shown by monitoring the birefringence of the solution using cross polars. The improved polymer alignment in solution has been preserved for several weeks after the end of shearing or of the application of the magnetic field.--

Please replace the paragraph beginning at page 8, line 21, with the following rewritten paragraph:

--For example, we have found that the rationally designed peptide P11-3 (SEQ ID NO: 3) in low ionic strength media at pH=7.5 does not self-assemble (peptide concentrations up to 10mg/ml). However, when 145mM NaCl is added in the solution or when the peptide is dissolved in cell media, it forms twisted beta-sheet fibrils, with narrow width of 4-5nm, wide width of 12-15nm, full pitch of 200-300nm, and length of several micrometers (Fig. 6).--

Please replace the paragraph beginning at page 9, line 6, with the following rewritten paragraph:

--Similar behaviour was found for the rationally designed peptide P11-5 (Table 1; SEQ ID NO: 5) in cell media. The main difference between fibrils of P11-3 (SEQ ID NO: 3) and of P11-5 (SEQ ID NO: 5) is that those formed by P11-3 (SEQ ID NO: 3) have a net –2 negative charge per peptide at pH=7.5, whilst those formed by P11-5 (SEQ ID NO: 5) have net +2 charge per peptide at pH=7.5. --

Please replace the paragraph beginning at page 9, line 17, with the following rewritten paragraph:

--The fibrils and gels of P11-3 (SEQ ID NO: 3) and P11-5 (SEQ ID NO: 5) in cell media were found to reform after sterilisation using an autoclave. Thus autoclave seems to be a viable method to sterilise these peptide gels. This is very significant, since sterilisation is a prerequisite for the use of these materials with cells *in vitro* or *in vivo*. Other alternative sterilisation methods that can also be used are filtration of the initially monomeric peptide solutions or gamma irradiation. Indeed we have found that the use of gamma irradiation sterilisation is preferred since it provides a clean, straightforward and reproducible method of sterilisation. Thus, in this

preferred aspect of the invention, the peptides may be dried to a powder and the dry peptide powder is subject to gamma irradiation.--

Please replace the paragraph beginning at page 10, line 13, with the following rewritten paragraph:

--Injection of P11-3 (SEQ ID NO: 3) and P11-5 (SEQ ID NO: 5) peptide solutions in cell media in mice has shown no effect of the presence of the peptide in the tissue surrounding the injection site as judged by histology after two and eight weeks following the peptide injection.--

Please replace the paragraph beginning at page 11, line 13, with the following rewritten paragraph:

--Peptides P11-6 (SEQ ID NO: 6) and P11-7 (table 1; SEQ ID NO: 7) on their own in cell medium do not self-assemble to form long beta-sheet polymers, and for this reason their solution in cell media is fluid-like rather than gel-like. Their lack of self-assembly is attributed to their high net positive and negative charges per peptide P: -4 for P11-6 (SEQ ID NO: 6) and +4 for P11-7 (SEQ ID NO: 7). When solutions of these two peptides in cell media (peptide concentration higher than 10mg/ml) are mixed together they spontaneously transform into a self-supporting gel, owing to the formation of heteropeptide beta-sheet polymers by these complementary interacting peptides.--

Please replace the paragraph beginning at page 19, line 23, with the following rewritten paragraph:

--Although a variety of peptides may be used, one such peptide which may be mentioned is the P11-3 peptide (SEQ ID NO: 3). A preferred group of peptides which may be mentioned are those selected from P11-1, P11-2, P11-3, P11-4, P11-5, P11-6 and P10-7 (SEQ ID NOS: -1-7, respectively).--

Please replace the paragraph beginning at page 20, line 19, with the following rewritten paragraph:

--Peptides were synthesised using standard 9-fluorenylmethoxycarbonyl (FMOC) chemistry protocols as described in A. Aggeli et al, J. Mat. Chem., 1997. P_{11}-2 (SEQ ID NO: 2),

P_{11}-3 (SEQ ID NO: 3) and P_{11}-5 (SEQ ID NO: 5) were purified by reversed-phase HPLC using a water-acetonitrile gradient in the presence of 0.1 % trifluoroacetic acid. Mass spectrometry showed the expected molecular weights (P_{11}-2: m/z 1594, P_{11}-3: m/z 1593, P_{11}-5: m/z 1523). P_{11}-4 (SEQ ID NO: 4) was purified by reversed-phase HPLC using 0.1 % ammonia in water as buffer A and 10 % buffer A in acetonitrile as buffer B. Mass spectrometry showed the expected molecular weight m/z 1596. --

Please replace the paragraphs beginning at page 21, line 5, with the following rewritten paragraphs:

--A rationally designed self-assembling peptide P11-3 (SEQ ID NO: 3) that forms solid-like gel network of interconnected negatively charged fibrils in cell culture medium

The rationally designed peptide P11-3 (Table 1; SEQ ID NO: 3) was dissolved in 145mM NaCl, pH~7.5 aq. solution (i.e. the ionic strength and pH values of the solution were similar to those present in cell culture medium) or it was added directly in cell culture medium. It was found that in both solutions, P11-3 (SEQ ID NO: 3) self-assembled into twisted beta-sheet fibrils, which had typically narrow width of 4-5nm, wide width of 12-15nm, full pitch of 200-300nm, and length of several micrometers (Fig. 6).--

Please replace the paragraphs beginning at page 21, line 25, with the following rewritten paragraphs:

--A rationally-designed self-assembling peptide P11-4 (SEQ ID NO: 4) that forms solid-like gel network of interconnected positively charged fibrils in cell culture medium

The rationally designed peptide P11-5 (Table 1; SEQ ID NO: 5) was dissolved in 145mM NaCl, pH~7.5 aqueous solution (i.e. the ionic strength and pH values of the solution were similar to those present in cell culture medium) or it was added directly in cell culture medium. It was found that in both solutions, P11-5 (SEQ ID NO: 5) self-assembled into twisted beta-sheet fibrils, which had typically narrow width of 4-5nm, wide width of 12-15nm, full pitch of 200-300nm, and length of several micrometers.

The main difference between fibrils of P11-3 (example 1; SEQ ID NO: 3) and of P11-5 (SEQ ID NO: 5; example 2) is that those formed by P11-3 (SEQ ID NO: 3) have a net negative

charge (-1 or –2) per peptide at pH=7.5, whilst those formed by P11-5 (SEQ ID NO: 5) have net positive (+1 or +2) charge per peptide at pH=7.5.

The fibrils of P11-5 (SEQ ID NO: 5) entwined partly with each other forming a three dimensional network and turned the peptide solution in cell media into a homogeneous self-supporting gel at peptide concentration higher than 15mg/ml. The gel remained stable for at least several weeks at room temperature.--

Please replace the paragraphs beginning at page 22, line 19, with the following rewritten paragraphs:

--Two rationally-designed self-assembling peptides P11-1 (SEQ ID NO: 1) and P11-2 (SEQ ID NO: 12 that form insoluble polymers that flocculate out of cell culture medium

The rationally designed peptides P11-1 and P11-2 (Table 1; SEQ ID NOS: 1 and 2, respectively) were dissolved independent of each other in 145mM NaCl, pH~7.5 aq. solution (i.e. the ionic strength and pH values of the solution were similar to those present in cell culture medium) or added directly in cell culture medium. It was found that in both solutions, both peptides self-assembled into elongated beta-sheet polymers, but these polymers were insoluble in cell culture medium solution conditions so they rapidly flocculated out of solution, causing the solution to be a turbid fluid. Consequently these peptide polymers did not give rise to self-supporting gels in cell culture medium .

The main difference between polymers formed by either P11-3 (example 1; SEQ ID NO: 3) or P11-5 (example 2; SEQ ID NO: 5) and those formed by either P11-1 (SEQ ID NO: 1) or P11-2 (SEQ ID NO: 2) is that the former had a significant net charged whilst the latter were practically neutral in cell culture medium. The net charge carried by either P11-3 (SEQ ID NO: 3) or P11-5 (SEQ ID NO: 5) polymers caused them to repel each other and thus to remain soluble and gel the cell culture. The absence of net charge on P11-1 (SEQ ID NO: 1) or P11-2 (SEQ ID NO: 2) caused them to be insoluble and thus not to form a gel in cell culture medium conditions. --

Please replace the paragraphs beginning at page 23, line 10, with the following rewritten paragraphs:

--Two rationally-designed complementary self-assembling peptides P11-5 (SEQ ID NO: 5) **and P11-6** (SEQ ID NO: 6) **that upon mixing, form solid-like gel in cell culture medium**

Peptides P11-6 and P11-7 (table 1; SEQ ID NOS: 6 and 7, repsectively) on their own in cell medium did not self-assemble to form long beta-sheet polymers, and for this reason their solutions in cell media remained fluid rather than gel. Their lack of self-assembly is attributed to their high (compared to P11-3 or P11-5 (SEQ ID NO: 3 and 5, respectively) net positive and negative charges per peptide : -4 for P11-6 (SEQ ID NO: 6) and +4 for P11-7 (SEQ ID NO: 7). When solutions of these two peptides in cell media (peptide concentration higher than 10mg/ml) were mixed together, the combine solution spontaneously transformed into a self-supporting gel, owing to the formation of heteropeptide beta-sheet polymers by these complementary peptides (Fig.3). --

Please replace the paragraph beginning at page 24, line 1, with the following rewritten paragraph:

--The P11-3 self assembling peptide (structure given in Table 1 and SEQ ID NO: 3) was assembled into its gel form by mixing with a solution supersaturated with respect to hydroxyapatite at pH 7.4 . The P11-3 (SEQ ID NO: 3) gel was incubated for 7d at 37oC. The gel was then washed and prepared for TEM, EDX and electron diffraction analyses. TEM showed deposits of electron dense, crystal-like material. Electron diffraction and EDX showed that the electron-dense material was apatitic (Ca:P = 1.66).--

Please replace the paragraph beginning at page 24, line 14, with the following rewritten paragraph:

--Gelatin was mixed with a solution supersaturated with respect to hydroxyapatite at pH 7.4 . The resultant gel had similar viscosity and organic concentration to the P11-3 (SEQ ID NO: 3) gel described in the previous example. The gelatin gel was incubated for 7d at 37oC. The gel was then washed and prepared for TEM, EDX and electron diffraction analyses. TEM showed no crystalline deposits in the gel.--

Please replace the paragraph beginning at page 26, line 26, with the following rewritten paragraph:

--Table 1 (SEQ ID NOS: 1-7): --

Please add the enclosed sequence listing to the specification.